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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,208	07/20/2001	Jiro Hitomi	MM4454	4894
79681	7590	11/19/2009		
David A. Einhorn, Esq. Baker & Hostetler LLP 45 Rockefeller Plaza New York, NY 10111			EXAMINER HADDAD, MAHER M	
			ART UNIT	PAPER NUMBER
			1644	
			MAIL DATE	DELIVERY MODE
			11/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/910,208	Applicant(s) HITOMI ET AL.	
	Examiner Maher M. Haddad	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-26 is/are pending in the application.
- 4a) Of the above claim(s) 24-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22 and 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/8/09, is acknowledged.
 2. Claims 22-26 are pending.
 3. Claims 24-26 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
 4. Claims 22-23 are under consideration in the instant application as they read on an antibody with binding affinity to a protein encoded by SEQ ID NO: 1.
 5. Applicant's statement that SEQ ID NO: 19 correspond directly to SEQ ID NO: 1 as identified in the application as originally filed, and corresponds to SEQ ID NO:19 in the Amendment dated March 7, 2007 is not clear. Applicant did not account for the single amino acid change in SEQ ID NO: 19. The encoded amino acid sequence by SEQ ID NO:1 comprises Gln at position 17, however, the newly added SEQ ID NO:19, filed on 3/27/07, has Glu at position 17. Accordingly, it is not clear what did applicant mean by "correspond directly".
 6. The specification stands objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Figures 1-2, on page 3, lines 15-32 has describe the amino acid sequence of bovine calcium-binding protein that must have a sequence identifier. Correction is required. The amendment to the specification filed 9/22/05 fails to provide sequence identifier for the amino acid sequence of the bovine calcium-binding protein in figure 1.
- Applicant's arguments, filed 9/08/09, have been fully considered, but have not been found convincing.
- Applicant fails to provide a sequence identifier for the bovine calcium-binding protein amino acid sequence in Fig. 1-2.
7. The amendment filed 9/22/05 and 3/27/07 stand objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

- i) The amendment filed on 3/27/07 to the computer readable form of the "Sequence Listing" with SEQ ID NO: 19 and 20 represents a departure from the specification and the claims as originally filed. Applicant does not point out for support for the newly added sequences. It is noted that the new SEQ ID NO: 19 contains ¹⁷Glu, which was not found in original SEQ ID NO: 19 (¹⁷Gln). Further, new SEQ ID NO: 20 contains ⁶⁵Asn, which was not found in original SEQ ID NO: 20 (⁶⁵Gln). The

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specification and the claims as originally filed have no support for the new replacement of SEQ ID NO: 19 and 20.

- ii) Further, it is noted that the amendment to the specification filed 9/22/05 to page 3, ¶5 (Fig. 2), points to SEQ ID NO:2 as the amino acid sequence of bovine calcium-binding protein. However, SEQ ID NO: 2 is only 50 amino acids in length and do not correspond to the nucleic acids sequence in figures 1 or 2.
- iii) The amendment filed on 9/22/05 to the specification on page 5, ¶3, substituting SEQ ID NO:1 or 12 for SEQ ID NO: 19 or 20 represents a departure from the specification and the claims as originally filed. The specification and the claims as originally filed have no support for the new replacement of SEQ ID NO: 1 or 12 with SEQ ID NO: 19 or 20. It is noted that there is no 1:1 correspondence between SEQ ID NO: 1 or 12 and SEQ ID NO: 19 or 20, respectively.

Applicant's arguments, filed 9/08/09, have been fully considered, but have not been found convincing.

Applicant submits that the statement of the Examiner regarding so-called "added material" not being supported by the original disclosure is inconsistent with the Declaration signed by Applicant. Applicant has already pointed out that there were some inconsistencies in a prior Amendments filed in November 2006. To overcome this inconsistency, Applicant has submitted a Declaration attesting to this fact. The Applicant has stated that the Amendment on March 7, 2007 is not a departure from the specification and claims as originally filed SEQ ID NO: 19 (¹⁷Gln) is correct and Applicant is attesting to this as being correct. This is also consistent with Figure 1, which is not in error and is consistent with the Amendment filed on March 7, 2007. Applicant has not added a new sequence for SEQ ID NO: 19. Accordingly, there is a 1:1 correspondence between SEQ ID NO: 1 and SEQ ID NO: 19 and no discrepancy exists with Fig. 1 and the patented SEQ ID NO: 19 in US. Patent No. 5,976,832.

Applicant submits that since Applicant in his Declaration and as set forth in the clean copy of the sequence listing for parent application Serial No. 08/568,310 involved in patent interference 105,501 clearly shows a match between SEQ ID NO:19 of the subject application as originally filed, and between SEQ ID NO: 19 of the priority application, no additional corroborating evidence is believed necessary to overcome the objection to the specification under 35 USC 132. No evidence other than the Declaration filed by Applicant and the clean copy of the sequence listing from the patent interference 105,501, as attached hereto, need to be presented to corroborate the accuracy of the sequence listing for SEQ ID NO: 19.

SEQ ID NO:19 depicts ¹⁷Glu (filed March 27, 2007)

<400> 19

```
Met Thr Lys Leu Glu Asp His Leu Glu Gly Ile Ile Asn Ile Phe His
1          5          10          15
```

```
Glu Tyr Ser Val Arg Val Gly His Phe Asp Thr Leu Asn Lys Arg Glu
20          25          30
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SEQ ID NO: 1 depicts ¹⁷Gln (filed March 27, 2007)

```

<400> 1
ctggcatgcc acacttctgt gcagaggggt gaacgtagtt tggtaaa atg act aag      56
                                     Met Thr Lys
                                     1

ctg gaa gat cac ctg gag gga atc atc aac atc ttc cac cag tac tcc      104
Leu Glu Asp His Leu Glu Gly Ile Ile Asn Ile Phe His Gln Tyr Ser
      5              10              15

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While Applicant admits that position 17 of SEQ ID NO:19 is Gln, however, the amendment filed March 27, 2007, lists position 17 of SEQ ID NO:19 as Glu. ¶12 of Second Declaration of David J. Weber, Ph.D., lists position 17 of SEQ ID NO:19 as Q (Gln). The "clean comp of SEQ ID NO: 19, filed in the patent interference No. 105,501, dated 10/16/2006, lists position 17 of SEQ ID NO:19 as Q (Gln). Yet, SEQ ID NO:19, filed 9/27/09, lists position 17 of SEQ ID NO:19 as Glu. Given the discrepancy between SEQ ID NO: 19, and the encoded amino acids sequence of SEQ ID NO: 1 with respect to position 17, it is not clear to the Examiner what is meant by "SEQ ID NO:19 ...correspond directly with the sequence listing of SEQ ID NO:1" in ¶3 of Dr. Hitomi declaration, filed 12/04/08.

Applicant fail to address the all the issues listed as i)-iii) in the previous Office Action mailed, 4/08/09. The objection is maintained for the reasons of record.

8. In view of the amendment filed on 9/08/09, only the following rejections are remained.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 22-23 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed. *This is a New Matter rejection for the following reasons:*

The phrases "SEQ ID NO: 19" claimed in claims 22-23 and "these lineages" claimed in claim 22, line 3 represents a departure from the specification and the claims as originally filed for the same reasons set forth in the previous Office Action mailed 4/08/09.

Applicant's arguments, filed 9/08/09, have been fully considered, but have not been found convincing.

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Applicant is attesting to the original listing of SEQ ID NO: 19. Applicant submits that there is no newly-added SEQ ID NO:19 and the original SEQ ID NO:19 (¹⁷Gln) is supported by the original specification. Applicant is not claiming or asserting that a new SEQ ID NO: 19 exists with (¹⁷Glu).

While applicants attesting to the original listing of SEQ ID NO:19, however, it is not clear what applicant is attesting to since there is no structure to SEQ ID NO: 19, to which they attesting. It appears that Applicant argues that instant SEQ ID NO:19 is the original sequence. However, SEQ ID NO: 19 cannot be found in the original filing of the application.

Applicant fails to address the limitation “these lineages” the rejection is maintained for the reasons of record.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 22-23 stand rejected under 35 U.S.C. 102(b) as being anticipated by Kelly *et al* (J. Pathol. 1989) as is evidenced by Guignard *et al* (Feb 1996).

Kelly *et al* teach monoclonal antibodies to study the expression of calgranulins by keratinocytes in inflammatory dermatoses. Kelly *et al* also teach that calgranulins are intracellular calcium binding proteins which have inflammatory cytokine activity. Further, Kelly *et al* teach that MAC 387 monoclonal antibody that recognizes a molecule probable containing both calgranulin A and B (see abstract in particular). MAC 387 monoclonal antibody also binds amino acid sequence encoded by SEQ ID NO: 19, as is evidenced by Guignard *et al* (Feb 1996) that the immunoreactivity of MAC 387 was compared with that of a polyclonal antibody raised against purified MRP-8, but cross-reacting with MRP-14, and p6 (hCAAF1/S100A12), a novel S100 protein. Under such conditions, Mac 387 was found to recognize the three S 100 proteins (see abstract in particular). Guignard *et al* concluded that the MAC 387 might recognize an epitope common to the proteins of the S100 family (see abstract last sentence). Guignard *et al* teach that all the S100 proteins have amino acid sequence and secondary-structure similarities in very specific and conserved regions which are the N- and C-terminal hydrophobic amino acid domains. They are also characterized by the presence of two calcium-binding sites called EF-hand, that contain 14 and 12 amino acids. Interestingly, the 14 amino acid EF-hand is conserved in all S100 proteins and is located in a conserved basic domain near the N-terminal part of The protein while the 12 amino acid EF-hand is located in a conserved acidic domain in the C-terminal region. These similarities make the generation of specific antisera difficult due to structural conservation and might explain the cross-reactivity of Mac 387 with MRP-14, MRP-8 and P6. If this mAb recognizes an epitope common to the proteins of S100 family, its use might allow the diction of novel members of this family (see page 106, under Discussion). Given that the human an bovine CAAF1 share 66% sequence homology, the reference MAC 387 would bind the claimed bovine sequence of SEQ ID NO:100, in the absence of evidence to the contrary.

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Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibody does not bind to the SEQ ID NO:19 recited in the claim. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Applicant's arguments, filed 9/8/09, have been fully considered, but have not been found convincing.

Applicant submits that nowhere is there any teaching of a nucleic acid or amino acid sequence in Guignard or Kelly nor has the Examiner made any allegation that any of the cited references teach an antibody specific to a calcium-binding protein comprising amino acid sequence shown by SEQ ID NO: 19. Both of these references describe the antibodies and proteins, but nowhere is there any mention of the antibodies specific to the respective sequences. The Examiner uses Yamamura to help support this argument, and while it is not being relied on for the actual anticipation rejection, the reference itself is from 1996. Applicant points out that this application claims priority to its parent which issued as USP 5,976,832 and was filed on December 6, 1995, which ultimately claims priority to JP 7-045564 and JP 7-070468, which were filed on March 6, 1995. Therefore, Applicant believes that Yamamura cannot be used as a reference under this section of the statute.

However, Applicant's argument attempts to limit the term "specific to a calcium-binding protein" of SEQ ID NO: 19, or encoded by SEQ ID NO: 1 in a manner inconsistent with the well-known and art-recognized specificity of antibody interaction with epitopes defined by particular amino acid sequences. That an antibody "cross-reacts", i.e., binds to more than one protein sequence base on shared epitope, does not mean that the antibody does not "specifically react" with both proteins. As is evidence by Guignard (1996), that the similarities among the S100 family proteins make the generation of specific anti-sera difficult due to structural conservation and might explain the cross-reactivity of Mac 387 with MRP-14, MRP-8 and P6.

Regarding Applicant's comment with respect to Yamamura reference, the examiner notes that the critical date of extrinsic evidence showing a universal fact need not antedate the filing date. See MPEP § 2124.

Applicant's comment with respect to the interference No. 105,501 is acknowledged. However, it is noted that said interference concerned with the protein of SEQ ID NO: 19. The claims are directed to antibodies not proteins. Antibodies are distinct from proteins. Further, in the antibody art, cross-reactivity of prior disclosed antibodies with SEQ ID NO: 19 and the protein encoded by SEQ ID NO: 1 read on the claimed invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 22-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Dell'Angelica (JBC, 269(46): 28929-28936, 1994) as evidenced by the specification disclosure on page 40, lines 6-9, Bost et al. (Immunol. Invest. 1988; 17:577-586), in view of Alisa Campbell (General properties and applications of monoclonal antibodies, Elsevier Science Publishers, 1984, section 1.1).

Dell'Angelica et al teach the primary structure (see Fig. 4) and binding properties of pig calgranulin C, S100-like calcium-binding protein from pig granulocytes. Dell'Angelica et al teach that the pig calgranulin C consists of 91 residues. Sequence analysis predicts two EF-band calcium-binding motifs (see Fig. 8), the first having an extended loop that is distinctive of the S100 protein family. Dell'Angelica et al teach that their results and the calcium-dependent binding of the protein to a phenyl-Superose column strongly suggest that calgranulin C undergoes a gross conformational change upon calcium binding thus supporting the idea that this protein may be involved in Ca²⁺-dependent signal transduction events (see abstract). The reference pig calgranulin C sequence has 79% sequence identity to claimed SEQ ID NO: 19. See below:

```
Qy      1  MTKLEDHLEGIINIFHEYSVRVGHFDTLNKRELKQLITKELPKTLQNTKDQPTIDKIFQD  60
      |||||:||||:|:|  |||||  ||:||||  |||||:
Db      1  MTKLEDHLEGIINIFHQYSVRLGHYDTLIKRELKQLITKELPNTLNKTKDQGTIDKIFQN  60

Qy      61  LDADKDGAVSFEEFVVLVSRVLKTAHIDIHKE  92
      |||:|  |||:|||||:  ||  ||  :|||
Db      61  LDANQDEQVSFKEFVVLVTVLITAHQNIHKE  92
```

The reference pig calgranulin C sequence has 81% sequence identity to claimed calcium-binding protein encoded by a nucleic acid sequence shown in SEQ ID NO: 1. See below:

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51ACTAAGCTGGAAGATCACCTGGAGGGAATCATCAACATCTTCCACCAGTACTCCGTTCCGGL10
   ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db   1  ThrLysLeuGluAspHisLeuGluGlyIleIleAsnIlePheHisGlnTyrSerValArg 20

Qy   111 GTGGGGCATTTTCGACACCCTCAACAAGCGTGAGCTGAAGCAGCTGATCACAAAGGAACCT
170
   :::|||||:::|||||||  ||||||||||||||||||||||||||||||||||||
Db   21  LeuGlyHisTyrAspThrLeuIleLysArgGluLeuLysGlnLeuIleThrLysGluLeu 40

Qy   171 CCAAAAACCTCCAGAACACCAAAGATCAACCTACCATTGACAAAATATTCCAAGACCTG
230

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          III  IIIII:::IIIIIIIIIIIIIIII  IIIIIIIIIIIIIIIIIIIII:::III
Db      41  ProAsnThrLeuLysAsnThrLysAspGlnGlyThrIleAspLysIlePheGlnAsnLeu 60

Qy      231  GATGCCGATAAAGACGGAGCCGTCAGCTTTGAGGAATTCGTAGTCCTGGTGTCCAGGGTG
290

          IIIII:::III  IIIIIIIIIIIIIIIIIIIIIIIIIIIIIII:::  III
Db      61  AspAlaAsnGlnAspGluGlnValSerPheLysGluPheValValLeuValThrAspVal 80

Qy      291  CTGAAAACAGCCACATAGATATCCACAAAGAG 323
          III  IIIIIIIIIII  :::IIIIIIIIIIIIIIII
Db      81  LeuIleThrAlaHisAspAsnIleHisLysGlu 91

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Dell'Angelica et al teach that both tryptic (T1-T11) and V8 protease (V1-V11) peptides were separated by RP-HPLC and subsequently submitted to amino acid analysis and/or Edman degradation (see fig. 3 and 4). Dell'Angelica et al teach that the sequence of T9 was identical to that of residues 1-17 (MTKLEDHLEGIINIFHEY, i.e., 100% identical to the N-terminus of the encoded peptide of SEQ ID NO:1) and was assumed to originate from a residual chymotryptic activity. Peptide T3 (QLITK) is 100% identical to the a peptide of SEQ ID NO: 19.

The claimed invention differs from the reference teachings only by the recitation of an antibody specific to a calcium-binding protein comprising an amino acid sequence shown in SEQ ID NO. or encoded by a nucleic acid sequence shown in SEQ ID NO: 1 in claims 22-23.

However, it has been held that once the antigen of interest is selected, the use of that antigen in the known method of Kohler and Milstein will result in the expected hybrid cell lines and the specific monoclonal antibodies. Ex parte Erlich, 3 USPQ2d 1011, 1015 (BPAI 1986).

Moreover, Campbell teaches that it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (see page 3 figure 11.1 in particular). One field of research in which monoclonal antibodies may prove of particular value is in the study of chromosomal proteins. The search for those chromosomal proteins which are responsible for determining cell phenotype has been particularly long and comparatively fruitless and monoclonal antibodies are ideal tools for the dissection of the complex mixture of proteins. As hybridoma production becomes a more routine laboratory technique (see page 29 and 30 under Basic research in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a monoclonal antibody as taught by Campbell against the pig calgranulin C or fragments thereof taught by Dell'Angelica et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because it was customary at the time the invention was made to make monoclonals against any new macromolecule as taught by Campbell.

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The resultant antibody would bind to the bovine CAAF1 of SEQ ID NO: 19 as is evidenced by Applicant's specification on page 40, lines 6-9 that the existence of antigen reacting with CAAF1-22-5 monoclonal antibody in human tissue strongly suggests the existence in human tissue of a protein (human CAAF1) homologous with bovine CAAF1. It is noted that human and bovine share only 66% sequence homology. Given the high sequence identity/homology between the referenced/claimed polypeptides (81% or 79%); the resultant antibodies would have the inherent property of binding bovine CAAF1 polypeptide of SEQ ID NO: 19 in the absence of objective evidence to the contrary.

Further evidence came from Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, mean that "specifically bind" with both proteins. Bost et al (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 9/08/09, have been fully considered, but have not been found convincing.

Applicant submits that as the Examiner has pointed out, since 21 amino acid residues of N-terminal are homologous between SEQ ID NO: 19 and Calgranulin and total homologous is 80%, therefore, there is a possibility that obtainable antibodies have cross-reactivity between SEQ ID NO:19 and Calgranulin C. This does not provide a basis for alleging obviousness since immunogens are different, monoclonal antibody specifically reactive to one of SEQ ID NO:19 and Calgranulin can be obtained.

It remains the Examiner's position that the resultant antibody would bind to the bovine CAAF1 of SEQ ID NO: 19. Further, Dell' Angelica et al teaches that the sequence of T9 was identical to that of residues 1-17 (MTKLEDHLEGIINIFHEY, i.e., 100% identical to the N-terminus of the encoded peptide of SEQ ID NO:1) and was assumed to originate from a residual chymotryptic activity. Peptide T3 (QLITK) is 100% identical to positions 34-38 of claimed SEQ ID NO:19 and the encoded amino acids of SEQ ID NO:1. The skilled in the art would target these peptide to make antibody and the resultant monoclonal antibody would bind both SEQ ID NO:19 and the encoded amino acids of SEQ ID NO:1.

15. No claim is allowed.

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16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 17, 2009

/Maher M. Haddad/
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